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(54) Composition for treatment of skin affections and process for its preparation.

(57) The invention is directed to a composition of skin disorders, such as cellulites or striae, comprising
- an oily fraction of paraffinic oils,
- an emulsifier, predominantly consisting of
  a) mono- and/or diglycerides of higher unsaturated natural fatty acids, and
  b) ethoxylated glycerides esterified with fatty acids,
- pancreas extract and/or thymus extract derived from pancreas and/or thymus tissue as such or from previously partially hydrolized pancreas and/or thymus tissue,
- stabilizer consisting of montmorillonites, the free oxygen sites of which have been covered with quaternary groups.
- a preservative consisting of esters of p-hydroxybenzoic acid and/or substituted imidazolidinyl urea derivatives, and
- water.

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Composition for treatment of skin affections and process for its preparation

The invention is relating to a composition for the treatment of skin affections and more particularly to a composition for treatment of so called skin disorders such as cellulitis or striae which affections seem both to be caused by a disturbed metabolism in the derm and usually manifest by means of an irregular shape of the epidermis and/or striking concentration of fatty tissue due to the absence or the destroyed state of connective tissue.

The invention is more relating to the application of such a composition for the fight against the beforementioned symptons and to a process for the preparation of such composition.

Already several means and compositions were proposed in the past for avoidance of such skin affections. However, with the formerly proposed means the prevention of the beforementioned symptons could not be attained. Therefore there is a still growing need for compositions for an efficient and quick treatment of the beforementioned skin disorders.

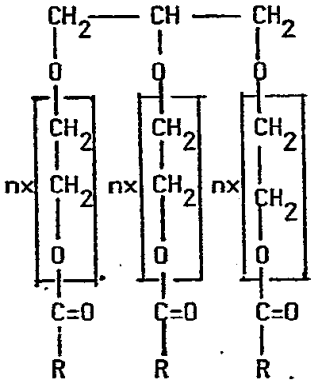
Surprisingly there could be found, as result of extensive research and experimentation, an adequate composition, which comprises at least the following ingredients:

- an oily fraction, consisting of optionally branched paraffinic oils containing 10-30 carbon atoms and preferably 12-25 carbon atoms in their chain, in an amount of 5-50% by weight and preferably by 10-30% by weight, calculated on the weight of the complete composition. The paraffinic oils have a boiling range of between 100 and 500°C and show a viscosity of up to 35 centistokes at 25°C.
  These paraffinic oils may optionally be mixed with esters from predominantly unsaturated higher natural fatty acids and from higher natural unsaturated aliphatic alcohols containing at most 20 carbon atoms, such as oleyl oleate or oleyl decalate (e.g. Cetiol V®).

By the term "higher natural fatty acids" and "higher natural" alcohols is meant fatty acids and alcohols, which may be derived from products occuring in nature, such as animal or vegetable oils and fats such as linseed oil, sunflower oil, rape-seed oil, whale oil, perilla seed oil, tung oil, castor oil.

It has appeared that for the most effective compositions, these esters have to be added to the paraffinic oil fraction in an amount of 1-6% by weight and preferably 2-5% by weight, calculated on the weight of the complete composition.

- an emulsifier, predominantly composed by
  a) mono- and/or diglycerides of higher unsaturated natural fatty acids, such as linoleic acid, oleic acid, linolenec acid, eleostearic acid, licanic acid, ricinoleic acid, petroselinic acid, vaccenic acid, arachidonic acid, cetoleic acid, erucic acid, selacholeic acid or palmitoleic acid or mixtures thereof, optionally mixed with those, derived from saturated higher natural fatty acids such as palmitic acid, lauric acid, miristic acid, stearic acid or mixtures thereof (e.g. Tegomuls®) in an amount of 1-10% by weight and preferably 2-8% by weight, calculated on the weight of the complete composition, and
  b) ethoxylated glycerides, esterified with fatty acids according to the general formula:



wherein n represents an integer from 5 to 20 and preferably 7-15, wherein R represents a saturated or unsaturated and preferably unsaturated fatty acid residue, derived from animal and/or vegetable oils, while R may represent the same or different fatty acid residues in one molecule but preferably the same residue (e.g. Tagat TO®).

In contradistinction to a large number of systems of a different kind which were empirically tried for this purpose, the beforementioned emulsifier system surprisingly appeared to meet the requirement, that not too large amounts are used of the inevitably to be applied emulsifiers with reference to skin affections on the one hand, as relatively small amounts of this emulsifier system appeared to be necessary as compared with the

presently proposed emulsifier system may be regarded according to the experience as extremely skin friendly which feature is related to a relatively low hydrophilic-lipophilic balance value.

The ratio between the amount of mono- and/or diglycerides on the one hand and the ethoxylated triglycerides on the other hand may vary, while the attractive activity is maintained, from 10-100 parts of mono- and/or diglycerides pro part of ethoxylated triglycerides and preferably 25 parts of mono- and/or diglycerides pro part of ethoxylated triglycerides.
The total amount of the beforementioned emulsifier system, calculated on the weight of the complete composition may vary from 1-10% by weight and preferably from 2-8% by weight for the most attractive results.

- pancreas and/or thymus extract derived from pancreas and/or thymus tissue as such or from previously partially hydrolyzed pancreas and/or thymus tissue and more particular from bovine pancreas and/or thymus.
  The pancreas extract to be applied is used in an amount of 3-5% by weight as dry matter based on the weight of the total composition and preferably used as a standard solution containing 10% by weight of pancreas dry matter (e.g. Revitalin®). Such a standard solution is added in an amount to give 0.05-5% by weight of pancreas dry matter material calculated on the weight of the complete composition and more preferably in an amount of 0.1-2% by weight.
  The thymus extract is applied in an amount of 0.01-5% as dry matter based on the weight of the total composition and preferably used as a standard solution containing 2,5-4% by weight of dry matter and preferably 3-3,5% of thymus dry matter in the form of thymus hydrolysate (peptide).

- a stabilizer, consisting of montmorillonites, the free oxygen sites of which have been covered with quaternary groups.
  Examples of such systems, which are preferably applied, are e.g. the so called Bentone® and Propoloid® preparations, which are added in an amount of 0.2-4% by weight and preferably of 0.5-2% by weight, calculated on the weight of the complete composition.

In the compositions containing the beforementioned stabilizers surprisingly no significant sagging occurs of one or more of the composing ingredients and particularly not in the relatively low viscous systems, which are preferred for practical reasons.

- a preservative. Preferably different types of preservatives are applied for the contineous oily phase and the dispersed aqueous phase. For instance an ester of parahydroxy benzoic acid and preferably the methyl and/or the propyl and/or butyl ester in an amount of from 0.05-1% by weight, calculated on the weight of the complete composition and preferably in an amount of from 0.2-0.4% by weight are to be applied in the oily phase. Preferably mixtures of methyl-, propyl- and butyl-p-hydroxybenzoate are applied (e.g. Phenonip®).
  These beforementioned preservatives may be replaced in total or partially by other preservatives primarily consisting of imidazolidinyl urea derivatives (e.g. Euxyl® 100 or Hydroconserv®) in an amount of from 0.05-1% by weight and preferably 0.2-0.4% by weight in the dispersed aqueous phase.
- water, ad 100% by weight, calculated on the weight of the complete composition.

In addition to the hereinbefore mentioned primary basic ingredients, one or more secondary ingredients may be added if desired, such as

- vitamin E as such or more preferably in the relatively stable acetate form, in an amount of 0.05-5% by weight based on the weight of the complete composition and more preferably in an amount of 0.2-2% by weight.
- glycerol as stabilizer of the emulsion, in an amount of 0.5-5.0% by weight, calculated on the weight of the complete composition, and preferably in an amount of 1-3% by weight.
- carraghenate, in an amount of from 0.1 to 5% by weight, calculated on the weight of the complete composition and preferably in an amount of from 0.5-2% by weight.
  The carraghenate, like e.g. Aubygum X®, is preferably consisting of a polysaccharide bearing sulfonic acid residues, being of natural origin such as those derived from sea weeds. The sulfonic acid residues optionally have been converted into salts or esters e.g. sodium salt or ester from glycol, propylene glycol and glycerol (so called modified carraghenates).
  Such carraghenates have empirically appeared to effect a surprisingly attractive stabilizing effect of the complete composition to be applied on the skin, while as additional advantageous effect, the known attractive properties of such carraghenates, such as elimination of an

eventual hardening of tissue, appeared to be maintained in the final complete system.

The hereinbefore mentioned amounts of carraghenate cause in the final composition a gel structure with a viscosity of from 200-5000 centipoises which is desired for an adequate application.

It will be appreciated by a person skilled in the art of this specific area, that the carraghenate possibly may partially be replaced by alternative gel forming means such as carboxymethylcellulose esterified polyacrylic acid (such as Carbopol®), hydroxy ethyl cellulose, in an amount which leads to a viscosity of the final composition in the same desired, hereinbefore mentioned specified range.

- perfume in an amount of from 0.1-0.5% by weight and preferably in an amount of 0.2% by weight, calculated on the amount of the total composition,
- an antioxydant in an amount of from 0.01-0.3% by weight and preferably in an amount of 0.1% by weight, calculated on the weight of the total composition.
- citric acid and optionally vitamin C, in an amount of 0.1-5% by weight calculated on the weight of the total composition and preferably in such an amount to give a pH of the total composition of a value from 5-8 and more particularly a normal pH of the outer skinlayers of from 5.5-7.5. It will be appreciated that the citric acid and/or vitamin C have to be added in the form of a buffer system, i.e. in partially neutralized form.
- alcohol (96%) in an amount of 0.1-1.0% by weight and preferably of 0.3-0.6% by weight, calculated on the weight of the total composition. The alcohol may be added for a fast gelation of the quaternary montmorillonites and preferably in an amount being the half of the amount of montmorillonites.
- camomile extract for giving the final composition the desired colour, in an amount of 0.01-0.5% by weight and preferably of 0.05-0.1% by weight, calculated on the weight of the complete composition (e.g. Azuleen®).

The present compositions are characterized in a relatively low viscosity and high stability and a fast curing of the beforementioned skin affections.

The compositions according to the present invention may be prepared according to a process, which forms another feature of this invention, the sequence of the addition and the rate of dosage of the respective components and the temperature of which have appeared to be important.
According to this process in a first step the complete continuous oily phase is prepared, composed by respectively the oil fractions, the esters of unsaturated fatty acids and alcohols, emulsifiers, stabilizers, preservatives and alcohol, while the dispersed aqueous phase in composed by water, glycerol, pancreas extract, the carraghenate, citric acid and/or vitamin C.
The vitamin E and camomile extract and perfume may be added to the prepared emulsion.
The final compositions of the present invention are preferably prepared by preparing and mixing the both phases at a temperature of at most 30°C, under addition of vitamin E, camomile extract and perfume and homogenizing the mixture.
The emulsion is additionally stirred and homogenized until an average size of the dispersed particles of at most 5 µ and preferably < 3 µ is reached.

It will be appreciated, that the process is characterized in a significant simplicity, which means a saving of labour and/or energy and therefore leads to lowered costs.

It will be appreciated that the treatment of the beforementioned skin disorders with the present compositions has to be regarded as one of the features of the invention.
Such a treatment is carried out in a way, usual for such compositions and is more particularly carried out by a process, characterized in that an amount of 2-5 ml is applied on the skin area involved and is spread evenly, optionally after thorough and careful cleaning of the skin with water and soap and/or an alcoholic solution.
This treatment has preferably to be carried out 2-3 times a day.

An additional advantage of such a treatment is caused by the fact that the skin area involved is not greasy rather immediately after treatment due to a fast penetration of the composition into the skin tissue. Therefore smudges in clothes or bed-linen may be avoided.

The invention is illustrated on basis of the subsequent examples, however without restricting the scope of it thereto:

Example 1

Under stirring the following ingredients are combined:

paraffinic oil (I) (Shell Ondina 15®, boiling range 295-390°C)	130 g.	oily phase
paraffinic oil II (Shell Ondina 68®, boiling range 290-500°C)	30 g.	
mono- and/or diglycerides (Tegomuls®)	25 g.	
oleyl decalate (Cetiol V®)	30 g.	
ethoxylated triglycerides (Tagat TO®)	1 g.	
preservative I (Phenonip®)	2 g.	
followed by addition of		
quaternary modified montmorillonites (Bentone 38®)	6 g.	
and gelation by		
addition of alcohol (96%)	3 g.	

The mixture is cooled to at most 30°C.

In water (632.5 g.) are subsequently dissolved:

preservative II (Euxyl 100®)	3 g.	aqueous phase
glycerol	20 g.	
pancreas extract (Revitalin® solution containing 10% by weight dry matter)	100 g.	
carraghenate (Aubygum X2®)	5 g.	

giving an aqueous phase, which is subsequently mixed with the obtained oily phase and homogenized after addition of vitamin E (10 g.), camomile extract (0.5 g.) and perfume (2 g.)

The obtained emulsion is further homogenized until an average particle size $< 3\,\mu$ is reached.

Example 2

In the same way as described under example 1, a composition is prepared from the following ingredients:

paraffinic oil I	125 g.	oily phase
paraffinic oil II	30 g.	
mono- and/or diglycerides	16 g.	
oleyloleate	26 g.	
ethoxylated triglycerides	1 g.	
preservative I	2 g.	
quaternary modified montmorillonites (Bentone 38®)	6 g.	
alcohol (96%)	3 g.	

and

water	610 g.	aqueous phase
glycerol	15 g.	
pancreas extract (Revitalin®, 10% solution)	150 g.	
preservative II	3 g.	
carraghenate (Aubygum X2®)	6 g.	

and

perfume	1 g.
vitamin E (acetate)	5 g.
camomile extract (azuleen)	1 g.

Example 3

In the same way as described in example 1, a composition was prepared from the following ingredients:

paraffinic oil I	160 g.	oily phase
paraffinic oil II	35 g.	
mono- and/or diglycerides	25 g.	
oleyldecalate	26 g.	
ethoxylated triglycerides	2 g.	
preservative I.	2 g.	
quaternary modified montmorillonites	7 g.	
alcohol (96%)	3 g.	

and

water	510 g.	aqueous phase
citric acid buffer, corresponding with		
citric acid	10 g.	
pancreas extract (Revitalon®, 10% sol.)	200 g.	
preservative III (Hydroconserv®)	3 g.	
carraghenate (Aubygum X2®)	10 g.	

and

perfume	1 g.
vitamin E (acetate)	5 g.
camomile extract (azuleen)	1 g.

Example 4

In the same way as described in example 1, a composition was prepared from the following ingredients:

paraffinic oil I	140 g.	oily phase
paraffinic oil II	25 g.	
mono- and/or diglycerides	15 g.	
oleyldecalate	26 g.	
ethoxylated triglycerides	0.5 g.	
preservative I	3 g.	
quaternary modified montmorillonites	7 g.	
alcohol (96%)	3 g.	

and

water	500.5 g.	aqueous phase
vitamin C and citric acid in a buffer form)	15 g.	
glycerol	20 g.	
pancreas extract (Revitalon®, 10% sol.)	200 g.	
preservative III	3 g.	
carraghenate (Aubygum X2®)	15 g.	

and

perfume	1 g.
vitamin E (acetate)	25 g.
camomile extract	1 g.

Example 5

In the same way as described in example 1, a composition was prepared from the following ingredients:

paraffinic oil I	130 g.	oily phase
paraffinic oil II	30 g.	
mono- and/or diglycerides	25 g.	
oleyl decalate	30 g.	
ethoxylated triglycerides	1 g.	
preservative I	3 g.	
quaternary modified montmorillonites	7 g.	
alcohol (96%)	3 g.	

and

water	666 g.	aqueous phase
citric acid in a buffer form	15 g.	
glycerol	20 g.	
thymus extract (3% solution)	35 g.	
preservative II	.3 g.	
carraghenate	15 g.	

and

perfume	1 g.
vitamine E (acetate)	15 g.
camomile extract	1 g.

Example 6

In the same way as described in example 1, a composition was prepared from the following ingredients:

paraffinic oil I	130 g.	oily phase
paraffinic oil II	30 g.	
mono- and/or diglycerides	25 g.	
oleyl decalate	30 g.	
ethoxylated triglycerides	1 g.	
preservative I	3 g.	
quaternary modified montmorillonites	7 g.	
alcohol (96%)	3 g.	

and

water	656 g.	aqueous phase
vitamin C and citric acid in a buffer form	15 g.	
glycerol	18 g.	
thymus extract (3% solution)	15 g.	
pancreas extract (10% solution)	50 g.	

and

perfume	1 g.
vitamin E	15 g.
camomile extract	1 g.

Claims

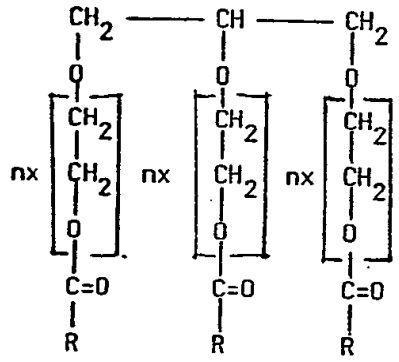
1. Composition for the treatment of skin disorders such as cellulites or striae, characterized in that it is least comprising the following ingredients:

- an oily fraction, consisting of optionally branched paraffinic oils containing 10-30 carbon atoms, in an amount of 5-50% by weight, calculated on the weight of the complete composition and optionally mixed with esters from predominantly unsaturated higher natural fatty acids and from higher natural unsaturated aliphatic alcohols containing at most 20 carbon atoms,

- an emulsifier, predominantly composed by

a) mono- and/or diglycerides of higher unsaturated natural fatty acids, optionnally mixed with those derived from saturated higher natural fatty acids, in an amount of 1-10% by weight, calculated on the weight of the complete composition, and

b) ethoxylated glycerides esterified with fatty acids according to the general formula



wherein n represents an integer from 5 to 20, wherein R represents a saturated or unsaturated fatty acid residue derived from animal and/or vegetable oils, while R may represent the same or different fatty acid residues in one molecule, whereby the ratio between the amount of mono- and/or diglycerides and the amount of ethoxylated triglycerides may vary from 10-100 parts pro part ethoxylated triglyceride, and whereby the amount of the emulsifier system, calculated on the weight of the complete composition may vary from 1-10% by weight.

- pancreas extract and/or thymus extract derived from pancreas and/or thymus tissue as such or from previously partially hydrolized pancreas and/or thymus tissue, in an amount of 0.05-5% by weight of pancreas dry matter material and/or an amount of 0.01-5% by weight of thymus dry matter material, calculated on the weight of the complete composition.
- stabilizer, consisting of montmorillonites, the free oxygen sites of which have been covered with quaternary groups, in an amount of 0.2-4% by weight, calculated on the weight of the complete composition
- a preservative, consisting of esters of para hydroxybenzoic acid and/or substituted imidazolidinyl urea derivates in an amount of 0.05-1% by weight, calculated on the weight of the complete composition
- water ad 100% by weight

2. Composition according to claim 1, characterized in that it contains in addition to the ingredients mentioned in claim 1, one or more of the following ingredients:

- vitamin E in an amount of 0.05-5% by weight based on the weight of the complete composition
- glycerol in an amount of 0.5-5% by weight,
- carraghenate in an amount of 0.1-5% by weight,
- perfume, in an amount of from 0.1-0.5% by weight,
- an antioxydant in an amount of o.1-0.3% by weight,
- citric acid and optionally vitamin C in an amount of 0.1-5% by weight,
- alcohol (96%) in an amount of 0.1-1.0% by weight,
- camomile extract in an amount of 0.01-0.5% by weight,

all percentages being calculated on the weight of the complete composition.

3. Composition according to claim 1, characterized in that it contains an oily fraction in an amount of 10-30% by weight.

4. Composition according to claim 1, characterized in that it is composed of an oily fraction, mixed with oleyl oleate or oleyl decalate, in an amount of 2-5% by weight, calculated on the weight of the complete composition.

5. Composition according to claim 1, characterized in that the emulsifier is composed of ethoxylated triglycerides and of mono- and/or diglycerides derived from linoleic acid, oleic acid, linolenic acid, or mixtures thereof, mixed with mono- and/or diglycerides derived from palmitic acid, lauric acid, miristic acid, stearic acid or mixtures thereof.

6. Composition according to claim 1, characterized in that the ratio between the amount of mono- and/or diglycerides and the ethoxylated triglycerides is 25 parts pro part ethoxylated triglycerides.

7. Composition according to claim 1, characterized in that as preservative in the oily phase one or more esters of p-hydroxybenzoic acid are applied in an amount of 0.2-0.4% by weight.

8. Composition according to claim 1, characterized in that as preservative in the aqueous phase imidazolidinyl urea derivatives are applied in an amount of 0.2-0.4% by weight.

9. Composition according to claim 1, characterized in that the pH of the complete composition is between 5.5 and 7.5.

10. Process for the preparation of a composition according to claims 1-9, characterized in that an oily phase is prepared by addition of the emulsifier, preservative and stabilizer to the oil components under stirring and heating and gelating after addition of alcohol, followed by cooling to 30°C or lower and followed by addition of an aqueous phase prepared by addition under stirring in water glycerol, pancreas extract, the carraghenate, citric acid and vitamine C buffer at a temperature of at most 30°C, followed by addition under stirring perfume and camomile extract, until an average particle size of at most 5 µ and preferably <3 µ is reached.

European Patent Office

EUROPEAN SEARCH REPORT

Application number

EP 85 10 6526

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.4)
A	EP-A-0 007 120 (CHEMISCH ADVIESBUREAU DRS. J.C.P. SCHREUDER) * Page 14, line 1 - page 15, line 6; claims 1-3 *	1-10	A 61 K 35/39 A 61 K 35/26 A 61 K 47/00 A 61 K 7/48
A	EP-A-0 048 153 (UNILEVER NV) * Page 20, claim 1 *	1-10	

TECHNICAL FIELDS SEARCHED (Int. Cl.4)

A 61 K

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	28-01-1986	BRINKMANN C.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
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P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
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